BIOTRUST RESEARCH MANUAL

Michigan BioTrust for Health

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INTRODUCTION

The Michigan Newborn Screening (NBS) Program began in 1965 and screens all babies born in the State of Michigan for more than 57 rare but serious disorders that benefit from early diagnosis and treatment. Currently, six drops of blood are collected from the heel of infants on filter paper and sent to the Michigan Department of Health and Human Services (MDHHS) laboratory for NBS testing. For more information, please visit the Michigan NBS program website.

Most dried blood spot (DBS) cards have whole or parts of spots that are left over after NBS testing is complete. Following recommendations from the Governor's Commission on Genetic Privacy and Progress, the Michigan Legislature amended the Public Health Code in 2000 to allow for the use of residual NBS blood spots in health research (MCL Section 333.5431). Subsequently, MDHHS developed the Michigan BioTrust for Health program to oversee the use of these residual specimens in medical and public health research studies.

The primary goals of the BioTrust are to: (1) make blood spots more useful for medical and public health research while protecting privacy, (2) encourage research, (3) engage and inform the public, and (4) allow personal decision-making. Since 2010, residual blood spots from NBS in Michigan have been used in more than 85 medical and public health research studies. A list of all research studies that have utilized these specimens is maintained online in the BioTrust Research Report.

This manual is intended for investigators interested in learning about utilizing DBS from the Michigan archive in research studies. It provides detailed information on:

- Availability of DBS for research.
- Consent requirements for accessing DBS.
- Storage conditions of archived DBS.
- MDHHS policies related to DBS research.
- Research application processes.
- DBS and data release processes.
- Charges related to DBS research.

THE MICHIGAN BLOOD SPOT ARCHIVE

The MDHHS residual DBS archive contains specimens from more than four million people born in Michigan in the past 35 years. Each year, approximately 100,000 DBS are collected for NBS and added to the archive after mandated testing is complete.

Due to the growing size and technical expertise required to maintain and store the DBS archive, MDHHS established a relationship in 2009 with a specialized storage facility—the Michigan Neonatal Biobank (MNB). The MNB is a non-profit organization located within Tech Town at Wayne State University with the sole purpose of securely maintaining Michigan's NBS residual DBS archive. It provides secure, temperature- and humidity-controlled environments for the archive. MNB receives DBS labeled with a code and is not granted access to any identifying information. MNB only releases blood spots to research studies under the direction and approval of MDHHS and the BioTrust program. For more information, please visit the MNB website.

After establishing the storage facility at MNB, MDHHS began transferring over legacy DBS cards already in storage. As of January 2026, over 4 million DBS have been sent to MNB for long-term storage, and work is ongoing to process and transfer the remaining samples physically located at MDHHS. MDHHS seeks to store DBS in conditions that best preserve the samples. Table 1 outlines current storage conditions of DBS cards based on the date of blood spot collection.

Table 1: DBS Storage conditions.

Date of DBS Collection:	Storage condition:
January 1987-December 1990	Destroyed after January 1st following the full 35-year retention period. Historically stored at MDHHS laboratory retention center in uncontrolled temperature/humidity environment or at MNB repository at ~70 degrees and ~35% humidity.
January 1991 through December 2008	Stored at MDHHS laboratory retention center in uncontrolled temperature/humidity environment or at MNB repository at ~70 degrees and ~35% humidity.
January 2009 through September 2010*	Stored in MNB repository. Specimens were frozen (-20C) within 90 days of collection for ~15 years then moved to ~70 degrees and ~35% humidity.
October 2010 to December 2011*	Stored in MNB repository. Specimens were frozen (-20C) within 14 days of collection for ~15 years then moved to ~70 degrees and ~35% humidity.
January 2012 to Current*	Stored in MNB repository. Specimens were frozen (-20C) within 14 days of collection.

Any specimen collected prior to January 2009 was originally stored in an uncontrolled temperature and humidity environment prior to shipment to MNB for long-term storage.

**Of note, any specimen collected between January 2009 and August 2012 and March 2020 through June 2020 may have undergone one to three freeze thaw cycles.*

GUIDELINES FOR THE RESEARCH USE OF BLOOD SPOTS

MDHHS maintains multiple policies that outline appropriate DBS storage and uses during the retention period. These policies are approved by the MDHHS Institutional Review Board (IRB) and the BioTrust Community Values Advisory Board (CVAB).

According to MDHHS policy HPL 111, DBS can be stored for up to 100 years, with the current MDHHS retention schedule stating that blood spots will be destroyed after 35 years. MDHHS policy HPE 114 outlines the acceptable uses of Michigan DBS in research studies. Below is a brief overview of this research policy. Researchers planning to request DBS for use in a research project must review this policy in detail.

Research priorities for Michigan blood spots include but are not limited to:

- Prenatal, childhood, or adult-onset disorders.
- Environmental exposures.

Research for the following purposes is expressly prohibited:

- Chemical, biological, or nuclear warfare.
- Cosmetics.
- Other non-health related ventures unless for purposes related to injury or medical conditions.

Protecting confidentiality in all BioTrust research activities is critical. **All research must be de-identified unless research teams obtain study-specific consent from each participant whose specimen they plan to access.** Study-specific informed consent must include a written signature from the participant or a legal guardian authorized to act on their behalf.

The use of DBS in genomic analyses is similarly limited. Researchers seeking approval to utilize DBS for whole genome or whole exome sequencing must obtain individual, study-specific, written consent prior to the release of specimens by MDHHS. Targeted DNA sequencing is permissible under BioTrust consent.

Prior to the release of any specimens for research purposes, investigators must first complete the BioTrust application process, described in detail within the Research application process section. Research projects that do not satisfy the criteria in policy HPE 114 will ***NOT*** be considered by MDHHS.

BLOOD SPOT AVAILABILITY AND CONSENT REQUIREMENTS

The availability of specific DBS for research depends upon the date that the sample was collected (Table 2), the approved study selection criteria, and the NBS program's discretion (e.g., DBS confirmed positive for a NBS condition may be deemed necessary for program quality improvement or assurance activities).

In compliance with the 35-year retention policy, DBS are prepared for destruction the January following their full 35-year retention period at which time they are no longer available for research use. Researchers are encouraged to consider potential impacts of annual destruction schedules on specimen selection and availability, recognizing that projects with older participants will be most significantly impacted. **Researchers will receive the oldest requested specimens, meeting their approved study selection criteria, that are *available at the time of specimen preparation and release*. DBS cannot be reserved beyond their retention period for any reason.**

Table 2: DBS availability.

Date of DBS Collection:	Availability of DBS for Research Purposes:
Between October 1987 and December 1990	Historically blood spots collected in this period were available for de-identified research under a waiver of informed consent granted by the MDHHS IRB. In compliance with the 35-year retention period policy, these spots are no longer available.
Between January 1991 and April 2010	Blood spots collected in this period are generally available for de-identified research under a waiver of informed consent granted by the MDHHS IRB. However, individuals have the option to opt out of blood spot research or to direct removal of their specimens from storage.
After May 2010	Blood spots are only available for use in de-identified research studies if a "Yes" BioTrust consent form decision is on file with MDHHS and has been verified. This consent is collected by hospital staff and home birthing attendants at the time of NBS blood spot collection. Individuals have the option to direct removal of their specimens from storage.

If planning a de-identified research study using DBS collected after May of 2010, it is important to consider that not all specimens are available, and this may affect random sampling techniques. As of December 2024, a "Yes" BioTrust consent form decision is documented for more than 936,979 specimens. Based on recent consent trends, it is estimated that a "Yes" consent will be available for approximately 50-60% of newborn screening specimens collected each year.

De-identified Research Studies

In de-identified research studies, the research team does not know whose DBS are included in the study. Only MDHHS possesses the ability to link the DBS with the identity of the person from whom the specimen originated; MNB does not have access to identifying information.

Due to internal quality assurance and quality control protocols, de-identified DBS are not available for research use until one full calendar year after their collection year, e.g., DBS collected in 2024 will be available for research release after January 2026.

Identified Research Studies

Investigators who wish to access DBS from specific individuals in an identified fashion must seek study-specific informed consent for such activities. Per BioTrust research policies, the consent must include a written signature from the participant or appropriate legal guardian. Consent forms must be reviewed and approved by the MDHHS IRB prior to use and must include sufficient language to describe the use of blood spots to the participant. Examples of language used in BioTrust-approved studies can be found in the appendix. Prior to the release of any specimens, a copy of each signed consent form must be provided to MDHHS for review along with identifiers used to link to the individual's DBS record.

Data Availability

Residual DBS from NBS can be linked to MDHHS data sets enabling research teams to select specimens based on set criteria or to include data in project analyses. All data released are de-identified unless research teams specifically seek informed consent from each participant to allow access to identified data elements. MDHHS will not release data to a research team until a data use agreement has been executed between MDHHS and the receiving institution(s). Inclusion of data sources beyond the NBS program may result in the need for additional approvals prior to execution of the study.

For further protection of confidentiality, de-identified data provided with DBS are subjected to BioTrust uniqueness testing protocols prior to release. In this process, the NBS epidemiologist ensures that the profile of data elements being released for sensitive variables match at least four other persons in the eligible study population. Sensitive variables considered for uniqueness testing include:

- Diagnosis with a disorder (e.g., NBS condition, broad category of cancer, presence of a congenital anomaly).
- Elements of dates including year, month, or day.
- Ages when coupled with elements of dates specific to year or smaller.
- Race, ethnicity, and ancestry information.
- Biological sex at birth.
- All elements of physical location. Information smaller than census tract will not be shared for any reason.
- Vital status.
- Receipt or enrollment in a public service program (e.g., Women, Infants, and Children [WIC], Medicaid, Medicare).

DBS have previously been linked to data from the following programs:

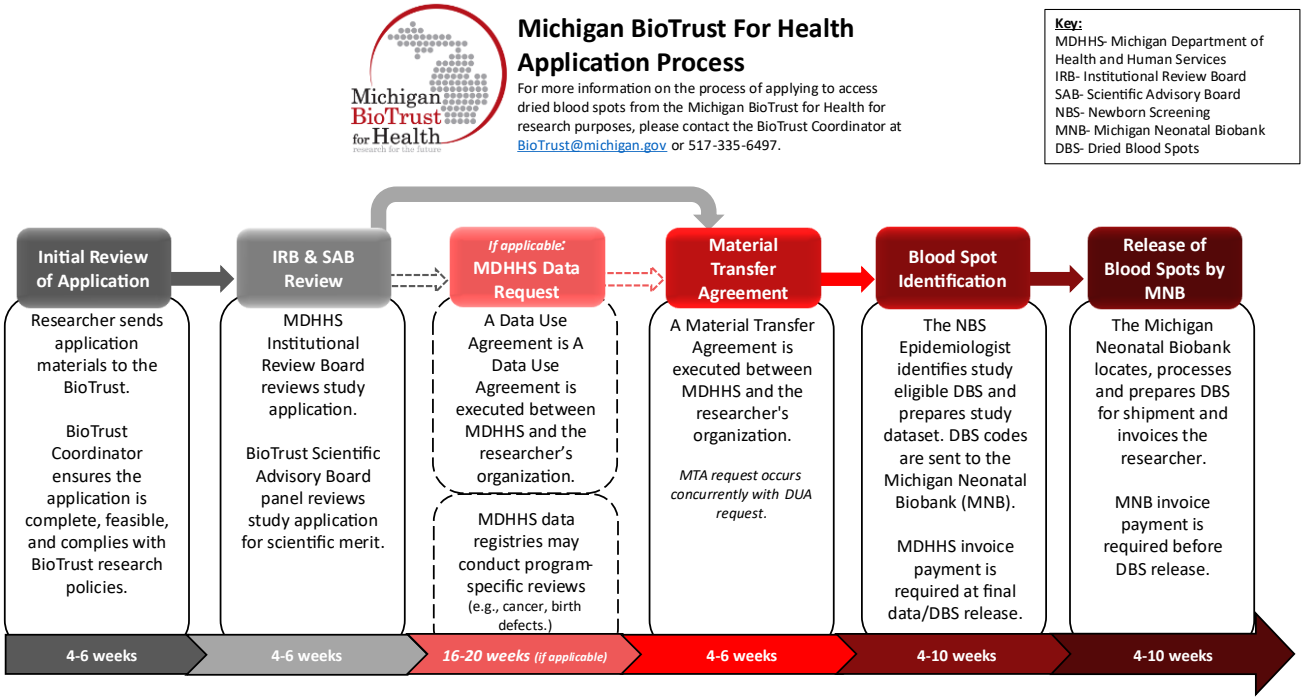
- **Newborn screening:** The Michigan NBS program maintains data related to the screening of all infants in the State of Michigan. The database includes demographic information, DBS characteristics and collection information, and analyte data for the screened conditions.
- **Vital Records (birth and death certificates):** This data source serves as an important source of statistical information related to births and deaths occurring in the state of Michigan. DBS have been linked to these records to allow for access to an expanded group of demographic, exposure, and outcome variables.
- **Michigan Cancer Surveillance Program (MCSP):** MCSP is a statewide, population-based cancer registry. Cancer cases are reported to MDHHS by health care providers throughout Michigan. DBS have been linked to MCSP records to identify specimens collected from people diagnosed with cancer.
- **Michigan Birth Defects Registry (MBDR):** The MBDR tracks diagnoses of birth defects in Michigan children. The registry currently tracks more than 1,000 diagnoses and has been linked to DBS to allow researchers to study children with birth defects in the state.
- **Medicaid claims:** These records document health care claims made for patients in Michigan who are covered by Medicaid insurance.

For more information on what may be included in these data sets, to request codebooks (where available), or to inquire about data availability from other sources, email the BioTrust research coordinator at BioTrust@Michigan.gov. For many of the listed data sources, availability also depends on the date of specimen collection, as data variables have changed over time.

If following the initial data release a researcher requests additional variables for de-identified research studies, MDHHS will work with the researcher to maintain subject anonymity. This may mean that variables need to be collapsed into categories or that certain variables cannot be provided.

RESEARCH APPLICATION PROCESS

MDHHS's review of a research study is multifaceted, and project materials are facilitated through the review process by the BioTrust research coordinator. DBS and data are not released for a specific research study until approval is granted by MDHHS and the appropriate agreements are executed. Figure 1 provides an overview of the steps required to access DBS and data from the Michigan BioTrust for Health. Additional details for each step are provided, including general timelines, which may be impacted by programmatic needs.



NOTE: Timelines are estimated and significantly depend on study complexity, project workload, and programmatic priorities.

Figure 1: Michigan BioTrust for Health research application process.

BioTrust Research Review Process

MDHHS Institutional Review Board (IRB)

The MDHHS IRB reviews each study requesting residual NBS DBS for adherence to ethical guidelines and to ensure that subjects' rights are adequately protected. The MDHHS IRB does not participate in reliance agreements for any studies using DBS. For additional information on the MDHHS IRB or to review monthly meeting dates, please visit the MDHHS IRB website.

- **Timeline:** The MDHHS IRB convenes on the first Tuesday of the month unless a schedule conflict is present. The schedule for MDHHS IRB meetings can be found online: IRB Monthly Meeting

Dates. Application materials must be submitted to the MDHHS IRB at least 10 business days prior to the next scheduled meeting. The BioTrust research coordinator requires materials 15 business days prior to the next IRB meeting to ensure adequate time to review materials for compliance with BioTrust policies. Please note that due to project complexity, 15 days is often inadequate time for the BioTrust research coordinator and research team to revise the application materials, if determined necessary prior to IRB submission.

BioTrust Scientific Advisory Board (SAB)

The BioTrust Scientific Advisory Board (SAB) evaluates each study protocol for scientific rigor, innovation and significance to health research, and feasibility and consistency with MDHHS policies regarding the appropriate research use of DBS. Reviewers employ a standard point scoring system ranging from one to seven, where one indicates the study has few strengths with numerous major weaknesses and seven indicates the study is extremely strong with negligible weaknesses. Review panelists are asked to score the project on a range of topics including whether the project has the ability to make original or significant contribution to the public's health or the understanding of the condition studied, whether the hypotheses and aims to be studied are clearly stated, and whether the proposed research is an appropriate use of residual DBS. Scores from all panelists are averaged to obtain a final study score. Proposals that receive an average composite score of 4.5 or higher and a recommendation for approval from a minimum of two reviewers will be considered approved, contingent upon MDHHS IRB approval. Proposals receiving a score of 4.4 or lower will be considered disapproved, however, protocols can be revised for further consideration.

- **Timeline:** Generally, SAB panel reviewers are given four to six weeks to complete their review, and the SAB Chairs are given an additional two weeks to confirm approval. All attempts are made to convene SAB reviews concurrent to IRB review, but timelines are dependent on reviewer availability, complexity of the application, and the number of applications in the queue at the time of submission.

Other MDHHS Program Advisory Boards

Additional MDHHS advisory boards and departmental approvals may be required for release of linked data, such as data from the Michigan Cancer Surveillance Program or the Birth Defects Registry. These review panels are convened once MDHHS IRB approval is granted. The need for these reviews will be communicated to individual research teams once project details and application materials have been shared with the BioTrust research coordinator. Although the BioTrust research coordinator will facilitate a review request, these reviews are managed and overseen by areas outside of the BioTrust.

Agreement Execution Process

The following agreements may be executed once all MDHHS boards have approved a research study:

Material Transfer Agreement (MTA)

A Material Transfer Agreement (MTA) specific to the research study is executed between the MDHHS Bureau of Laboratories and the research and/or testing laboratory for each institution receiving DBS or material derived from DBS testing. Following MDHHS approvals, the MTA will be drafted by the BioTrust research coordinator, reviewed and signed by the research/ testing institution, and then fully executed by the MDHHS Bureau of Laboratories.

- **Timeline:** Final MTA execution at MDHHS takes approximately two weeks.

Data Use Agreement (DUA)

A Data Use Agreement (DUA) is only executed for studies that request data from MDHHS program areas. Research studies requesting only DBS and no accompanying data are not subject to DUA requirements. Where necessary, the DUA is executed between MDHHS and the research organization(s). If a research study is requesting data elements, a DCH-1294 form will need to be included in the application materials. The BioTrust research coordinator will provide the necessary forms and facilitate with program areas outside of the NBS program as needed. Following MDHHS approvals, a project specific DUA will be drafted by the BioTrust research coordinator, reviewed and signed by the research or testing institution, and then fully executed by the MDHHS compliance office. DUAs expire three years from their execution date and must either be renewed or the researcher must provide an attestation of data destruction (MDHHS-6207 form).

- **Timeline:** The MDHHS compliance office will review initial DUA submissions within approximately two weeks. Final DUA execution at MDHHS takes approximately 5-10 business days.

Submitting a BioTrust Application

Below is an outline of all documentation necessary for an MDHHS research application submission for studies utilizing BioTrust specimens. The BioTrust review process is intended to review the entirety of the study, not just aspects related to DBS or MDHHS data analyses. Required forms can be downloaded from the Michigan BioTrust for Health - Dried Blood Spot Research webpage or can be requested by emailing the BioTrust research coordinator. BioTrust research applications can be submitted directly to the BioTrust research coordinator at BioTrust@michigan.gov. Once documentation for a study has been submitted, the BioTrust research coordinator will do an initial review of all documents. Following the initial review, the BioTrust research coordinator will respond with any questions about the application and an estimated timeline for review by both the MDHHS IRB and the BioTrust SAB. Each BioTrust research application must include the following materials:

MDHHS IRB Application

Two forms are available to request MDHHS IRB review: (1) the MDHHS IRB Initial Review Application (DCH-1277) or (2) the MDHHS IRB Abbreviated Initial Review Application (DCH-1277-A). If the research is being reviewed by another IRB, and the external IRB application specifically delineates how Michigan

DBS are going to be used, the researcher can submit the **full external IRB application** to MDHHS along with the MDHHS IRB Abbreviated Initial Review Application. If the research is not being reviewed by an external IRB or if the external IRB application does not clearly delineate how Michigan DBS are going to be used, the MDHHS IRB Initial Review Application should be utilized. Visit the MDHHS IRB webpage to view useful references for selecting an MDHHS IRB application.

In addition to the initial IRB application, the BioTrust research coordinator will facilitate annual IRB study renewals for the research team.

BioTrust Application Form

The BioTrust Application form requests specific details about the research study's proposed DBS use, including where DBS will be tested, the DBS quantity and size required for testing, any linked data requested, and a brief description of the study to be shared publicly in the online BioTrust Research Report. The final section of the BioTrust Application form includes a BioTrust application checklist.

Principal Investigator and Testing Scientist Curriculum Vitae (CV)

The SAB panel will consider the investigator's and testing scientist's experience to determine if project completion is feasible based on previous research activities and expertise.

PI and Testing Scientist Human Subjects Research Training

A copy of a human subjects research training certificate is required by the IRB. Information about the required human research protection training is maintained on the MDHHS IRB Required Human Research Protections Training webpage. In short, MDHHS will accept certificates from CITI Program trainings, those offered through the U.S. Department of Health and Human Services Office for Human Research Protections (OHRP), or through university established training programs.

Detailed Study Protocol

In addition to details on the entirety of the study (aims, study design, participant selection and/or enrollment, testing methodology, analyses), the protocol should clearly delineate how BioTrust DBS and MDHHS data will be utilized in the research study. Details on availability of resources to conduct the research should also be included.

Consent Forms or Other Study Documents

If the study is requesting identified DBS, identified data, whole-genome DNA sequencing, or whole-exome DNA sequencing, a copy of the informed study-specific consent form(s) must be included in the BioTrust application materials. Additional study documents, such as assent forms for minors, recruitment materials, surveys, or data collection tools, must also be included in the application.

BioTrust Application Checklist

For assistance with any of the application materials, please contact the BioTrust research coordinator at BioTrust@michigan.gov.

1. MDHHS IRB application (Full or Abbreviated).

2. BioTrust Application form.
3. Principal investigator's CV.
4. Principal investigator's human subjects research protection training certificate.
5. Testing Scientist's CV.
6. Testing Scientist's human subjects research protection training certificate.
7. Detailed and comprehensive study protocol.
8. Other study documents, as applicable.

Study Revision Process

Prior to implementing protocol changes or utilizing revised study materials, all study revisions must be reviewed and approved by the MDHHS IRB and BioTrust SAB Chairs. As with the initial application process, revision reviews apply to the entirety of the study, not just the aspects related to DBS or MDHHS data analyses. To initiate a revision application, the researcher should contact the BioTrust research coordinator at BioTrust@michigan.gov, who will facilitate the process of obtaining MDHHS approvals and revising and re-executing the MTA and DUA, as appropriate. Similar to the initial application process, the BioTrust research coordinator will do an initial review of all revised documents, respond to the researcher with any questions, and provide an estimated timeline for IRB and SAB Chair review. The BioTrust research coordinator will also facilitate review by other MDHHS program areas as necessary (e.g., MCSP SAB for studies receiving cancer data). Each BioTrust research revision application must include the following materials, submitted as files using track changes to indicate the proposed revisions:

1. MDHHS IRB revision form (DCH-1478).
2. Revised BioTrust Application form, with track changes.
3. Revised study protocol, with track changes.
4. Revised informed consent form(s), if applicable, with track changes.
5. Revised study materials, if applicable (e.g., assent forms, recruitment materials, surveys, data collection forms), with track changes.

POST-APPROVAL BLOOD SPOT AND DATA RELEASE PROCESS

Once a research study has received full MDHHS approvals and all necessary agreements have been executed, BioTrust staff will work with the research team, MNB, and other MDHHS programs, as applicable, to identify and prepare DBS and any associated data requested for the study. To initiate a study release, the research team will submit a BioTrust Request form to the BioTrust research coordinator, specifying details of the DBS and/or data quantity requested for release. The completion timeline for DBS and data preparation and release is largely dependent on study complexity, including sample size, consent verification and linkage, DBS eligibility criteria, study design (e.g., matched case control), and uniqueness testing.

DBS Eligibility and Linkage

The NBS epidemiologist will identify eligible DBS for each study based on the sampling frame and eligibility criteria specified within the approved study protocol and BioTrust Application. As needed, the NBS epidemiologist will coordinate with other MDHHS programs to obtain approved data.

For studies with approval to receive identifiable DBS or data, verification of each participants' study-specific consent will be conducted independently by two MDHHS staff prior to release. The research team will work with the BioTrust research coordinator to securely share the following information needed for linkage to the participants' DBS record:

1. A copy of the signed informed consent form for each participant whose DBS is requested.
    a. Include the research study ID in the filename of each informed consent form.
    b. Provide a copy of the signed assent form for each minor, if applicable, and note the assent parameters approved within the study protocol (e.g., both parental consent and participant assent was obtained for participating children 8-11 years old).
2. A spreadsheet with as many of the following elements as possible:
    a. Research study ID.
    b. Participant/child's full name at birth.
    c. Participant/child's name at consent/assent, if different than birth.
    d. Participant/child's date of birth.
    e. Participant/child's sex assigned at birth.
    f. Birth order, if applicable.
    g. Mother's full name at delivery.
    h. Mother/Guardian's name at consent, if applicable.

i. Hospital/location of birth.

j. Adoption/guardian status, if applicable.

DBS Preparation and Release

After the NBS epidemiologist identifies DBS meeting the study's criteria, the NBS epidemiologist will prepare a list of eligible DBS codes and the BioTrust research coordinator will send the list to the MNB to request sample preparation.

MNB staff will prepare DBS research samples based on the approved DBS quantity and size.

DBS and Data Release

MNB will label each DBS study sample and associated data with a study ID, removing the MDHHS DBS code. For de-identified research studies, this study ID will be assigned at random by the MNB and will not be related to any identifying information. Only the MNB will hold the link between the random study ID and MDHHS DBS code. For research studies requesting identifiable specimens and/or data, MNB will label each DBS study sample with the study ID provided by the research team to the BioTrust research coordinator for consent verification and linkage.

MNB will communicate directly with the research team and testing laboratory to confirm DBS and de-identified data release to the approved recipients, MNB invoicing, and DBS shipping details. The NBS Epidemiologist or BioTrust research coordinator will release identifiable study datasets to the approved recipient(s). MDHHS invoicing and payment will occur with each release of study data.

Manuscript Preparation and Results Publication

MDHHS requires review of near-final manuscripts prior to publication submission to ensure accurate descriptions of DBS and MDHHS data. When available, researchers will be asked to provide a brief lay summary of study results and/or link(s) to related publication(s) that can be added to the online BioTrust Research Report.

Study Closure

The BioTrust research coordinator will facilitate study closure activities for research teams whose study is completed or are no longer utilizing DBS specimens or MDHHS data. Study closure involves submission of the following forms:

1. MDHHS IRB study closure form.
2. MTA Appendix A, documenting destruction of DBS samples and derived materials.
3. DUA Attestation form (MDHHS-6207), documenting destruction of MDHHS data.
4. Lay summary of study results.

FEES ASSOCIATED WITH BIOTRUST RESEARCH

Costs associated with utilizing DBS from the Michigan BioTrust for Health archive for research are intended to recuperate staff time associated with study activities. Separate cost recovery estimates associated with MDHHS data requests and MNB DBS release will be provided to the research team following review of the initial application and revision applications, as needed.

MDHHS Cost Recovery Fees

MDHHS has implemented the following BioTrust cost recovery structure to recuperate costs associated with BioTrust and NBS staff time invested in securing approvals, executing agreements, and selecting specimens for use in research studies utilizing DBS through the Michigan BioTrust for Health. MDHHS does not profit from research using residual DBS. MDHHS program areas covered by the BioTrust cost recovery schedule include the Division of Lifecourse Epidemiology and Genomics and the Newborn Screening Section of the Division of Clinical Chemistry and Toxicology.

Under the BioTrust fee schedule, the following structure is used to estimate the cost recovery charge for each individual research request. The hourly rate is $75/hour.

- An application coordination charge of three hours at the hourly rate will be applied to each study. This charge is intended to recover the cost of staff time invested in ensuring that all regulatory approvals and agreement executions are obtained prior to the release of DBS and/or data for research use.
- The structure below is used to estimate additional costs associated with staff time based on the study protocol:
    - Random samples – cohort:
        - Three hours.
    - Random samples – case-control:
        - Six hours (includes matching on up to three variables).
        - One hour for each additional three matching variables.
    - Consented population:
        - Six hours (for up to 100 subjects).
        - One hour for every additional 100 subjects.
    - Linkage to any dataset:
        - Three hours per dataset.
    - Any additional variables:
        - One hour for every five variables.
    - Complexity charge(s): Additional hours will be charged for studies with unique/complex requests. Examples include:

- Time spent looking for diagnosed/positive cases.
- Time spent verifying data received from researchers.
- Time spent by NBS laboratory staff to process samples still in storage at MDHHS (one hour per 20 specimen).

An estimate for the MDHHS cost recovery charge will be provided for an individual research study upon request or at the time the full application is received for review by MDHHS. To request an estimate, please contact the BioTrust research coordinator at BioTrust@michigan.gov.

Cost recovery charges are assessed separately for data from MDHHS data systems or registries external to the NBS and BioTrust programs (e.g., Michigan Cancer Surveillance Program, Birth Defects Registry). The BioTrust research coordinator will facilitate estimates from the appropriate program areas upon request or at the time the full or revised application is received for review.

Michigan Neonatal Biobank Fees

The MNB charges an administrative fee to researchers utilizing DBS for MDHHS-approved research studies. This fee helps offset the cost of storage, labor, and shipping and is charged separately from the cost recovery charges issued by MDHHS for the BioTrust and other program areas, as applicable. For additional information or an estimate, please contact MNB staff at mnbb@wayne.edu.

APPENDIX

Study Specific Consent Examples

Below are three examples of language used in previous study-specific consent forms that describe the use of residual DBS to study participants. These are intended to be used as a starting point for developing language specific to your own project. All consent language must be reviewed by the BioTrust research coordinator and MDHHS IRB prior to being implemented in the field.

Example 1

In Michigan, a few drops of blood are collected from a baby's heel shortly after birth to diagnose disorders that need early treatment. This is called newborn screening. In this study, researchers will use blood spots that may be left over from newborn screening to measure [EXPOSURE/CONDITION] and compare that to your child's birth records and other information. This is a research study, which is different from MDHHS' routine public health activities.

By signing this Informed Consent document, you give us permission to access and test your child's leftover, unused newborn dried blood spot for [EXPOSURE/CONDITION]. Your child's leftover newborn dried blood spot will only be tested for [EXPOSURE/CONDITION]. We will not use this blood for alcohol, drug, or DNA testing.

> **What is an unused newborn dried blood spot?** The State of Michigan requires newborn dried blood samples to be collected at birth. These are used to learn if infants have rare diseases needing special care very early in life. Blood spots leftover after the screening are stored for quality assurance and can be made available for research through the Michigan BioTrust for Health (BioTrust). With your permission, we will use some of your child's newborn blood spots for this study. You can learn more about the BioTrust at http://www.michigan.gov/biotrust.

We will link previously collected birth and health information from your child to the results of [EXPOSURE/CONDITION] testing from your child's leftover newborn dried blood spot. **We will use this dataset to understand how some information we have collected may be related to other information we have collected, including if [EXPOSURE/CONDITION] may relate to certain [CONDITIONS]**.

A copy of your signed Informed Consent form (this document) will be shared with the BioTrust for approval to access your child's newborn blood spot. To access and locate your child's newborn blood spot, we will ask you to provide:

- Your child's name that was given at the time of their birth (the name on your child's birth certificate).
- The sex your child was assigned at birth.
- Your child's date of birth.
- The name of your child's birth mother.
- The date of birth of your child's birth mother.
- The name and address of the hospital or birth center where your child was born.

Example 2

By consenting to this study, you will provide research staff permission to access a sample of your child's already collected newborn blood screen (blood spot card) from the Michigan Department of Health and Human Services (MDHHS). For all births in Michigan, blood is collected from an infant shortly after birth to diagnose disorders that need early treatment. After the newborn screening is completed, the infant's dried blood spot samples that are leftover are stored by MDHHS. These blood spots can be used for research through the Michigan BioTrust for Health Program. We are requesting your permission to allow our research team the ability to access your child's identified blood spots. We need the blood spots to be identified so that we can connect this information to other information you may provide us during this research study. We will use a small portion from the leftover stored blood spots. Our purpose for the use of the blood spots is to analyze various [EXPOSURES/CONDITIONS] at the time of birth and their association with [CONDITION].

The research team will obtain your child's newborn blood screen from MDHHS. Your child's newborn blood screen was previously collected from your child when they were 24 hours old (while in the hospital after their birth) and is routinely stored by MDHHS. We will be requesting the use of leftover blood spot samples from MDHHS for further analysis as well as previously obtained [EXPOSURE/CONDITION] results.

Example 3

Neonatal Dried Bloodspots: If you were born in Michigan after October 1987, dried blood spots were collected following your birth. These blood spots have been taken from every newborn in the state of Michigan for many years in order to test for certain conditions that would require early treatment for the baby. After coding to protect your privacy, blood spots leftover after newborn screening can be used for research through the Michigan BioTrust for Health program. We are requesting your permission to have access to your identified leftover blood spots for this research. We will use the bloodspot sample to measure [EXPOSURE/CONDITION]. We will also use the dried bloodspot sample to analyze your genetic material. Genes are very small units of DNA that carry information about traits that are passed from parents to children. Scientists can learn about how genes are regulated and expressed, which affects traits and overall health, from samples of DNA obtained from blood. We only test for methylation – a regulator of genes that turns them on and off – of these genes and not the genetic sequence.

This analysis will be used only for research purposes. We will study your sample along with the samples from others in this study to see if there are exposures measured at the time of birth that are linked to [CONDITION] and other health conditions developing later in life. We will also study whether changes to gene regulation at the time of birth can tell us whether disease is likely to develop later in life. Data that we get from this study will be saved to be used in future studies as well. However, unused portions of the dried bloodspot itself will be sent back to the Michigan BioTrust for Health; it will not be used for any other study. You may still participate in the study without permitting us to access your neonatal blood spots.

Abbreviations

Common abbreviations used throughout this manual include:

Abbreviation	Meaning
CITI	Collaborative Institutional Training Initiative
CV	Curriculum Vitae
CVAB	Community Values Advisory Board
DBS	Dried Blood Spot(s)
DUA	Data Use Agreement
IRB	Institutional Review Board
MBDR	Michigan Birth Defects Registry
MCSP	Michigan Cancer Surveillance Program
MDHHS	Michigan Department of Health and Human Services
MNB	Michigan Neonatal Bank
MTA	Materials Transfer Agreement
NBS	Newborn Screening
PI	Principal Investigator
OHRP	Department of Health and Human Services Office for Human Research Protections
SAB	Scientific Advisory Board